

**REMARKS/ARGUMENTS****I. Introduction**

Receipt is acknowledged of the Final Office Action mailed July 30, 2003 (Paper No. 16). In response to the Examiner's restriction requirement, claims 34-43 and 57-59 were elected in Applicants' reply filed December 6, 2002. Claims 35, 44-56, and 58-59 were canceled, and claim 60 was added in Applicants' Amendment filed May 12, 2003. Currently, claims 34, 36-43, 57, and 60-61 are pending in the application. Claims 34, 36-43, and 57 have been amended. Claim 61 has been newly added. The specification has been amended to reflect the amended claims. Support for amended claim 34 can be found at page 8, line 39 through page 9, line 1. Support for amended claim 38 can be found at page 5, lines 3-10. Support for amended claim 57 can be found at page 1, lines 11-14 and page 8, line 39 through page 9, line 1. Support for new claim 61 can be found at page 4, line 26. No new matter has been added in the amendments, which are fully supported by the specification.

**II. Examiner's Rejections****A. Rejections Maintained Under 35 U.S.C. § 112, first paragraph**

The Examiner has maintained the rejection of claim 57 under 35 U.S.C. § 112, first paragraph, as lacking an enabling disclosure pertaining to vaccines. The Examiner argues that the specification fails to teach the necessary steps for preparation of the vaccine, the situations for use, guidelines for administration, criteria for administration of the vaccine, such as who would be a good candidate for such a vaccine, or a recommended amount of the vaccine for use in the treatment of diseases. The Examiner also alleges that the specification discloses that only dendritic cells in immature status are capable of taking up peptide antigens, and it is unclear as to

how matured dendritic cells may further uptake peptide fragments or antigens for presentation.

**B. Rejections Maintained Under 35 U.S.C. § 102(b)**

The Examiner has maintained the rejection of claim 34 under 35 U.S.C. § 102(b) as being anticipated by Wenge *et al.* The Examiner has stated that the Applicants' arguments that Wenge *et al.* teach a maturation process using high molecular weight hyaluronic acid fragments, while amended claim 34 recites low molecular weight hyaluronic acid fragments having a size of 2,000-5,000 Daltons (Da), are not found persuasive because the claims allegedly still read on hyaluronic acid proteins that are of a larger molecular weight because of the recitation of the term "comprises". The Examiner has stated that in the absence of evidence to the contrary, high molecular weight hyaluronic acid would inherently have at least 2-12 building blocks, given that smaller fragments have at least 2-12 building blocks.

The Examiner also has maintained the rejection of claim 57 under 35 U.S.C. § 102(b) as being anticipated by Noble *et al.* The Examiner has stated that Applicants' argument that Noble *et al.* teach hyaluronic acid fragments that are 200,000 Da, while that of the instantly claimed invention are 2,000-5,000 Da, are not persuasive for the same reasons that the Examiner rejected claim 34.

**III. Examiner's Objections**

The Examiner has objected to claims 35-43 and 60 as being dependent upon rejected base claim 34, but that claims 35-43 and 60 would be allowable if rewritten in independent form, including all of the limitations of the base claim and any intervening claims.

#### **IV. Applicants' Response to the Examiner's Rejections**

Applicants thank Examiner Yaen for the interview on October 14, 2003 and for the suggestions for putting this case in condition for allowance.

##### **A. Rejections Maintained Under 35 U.S.C. § 112, first paragraph**

In response to the Examiner's rejection of claim 57 under 35 U.S.C. § 112, first paragraph, as lacking an enabling disclosure, without acquiescing in the rejection, and in accordance with the Examiner's suggestions on October 14, 2003, Applicants have amended claim 57 to recite a pharmaceutical composition comprising the elements of amended claim 34. Thus, the Examiner's rejections are rendered moot by this amendment.

In response to the Examiner's argument that the specification is not enabled for using antigen presenting cells such as matured dendritic cells vs. immature dendritic cells for antigen uptake in the claimed pharmaceutical composition, Applicants note that while immature dendritic cells may be more efficient at binding to, up-taking, and processing antigens than matured dendritic cells, it is during the antigen uptake process that the immature dendritic cells mature and exchange their uptake efficiency for expression of more surface MHC class II molecules, to which the pharmaceutical composition, comprising hyaluronic acid fragments, may bind (page 28, lines 21-23; page 16, lines 13-17 of the specification). This increased binding produces increased T cell clustering stimulation, which in turn, produces an increased immune response (page 20, lines 8-11 of the specification). Thus, mature dendritic cells are desirable to use in the instant pharmaceutical composition because pre-treating and maturing immature dendritic cells with low molecular weight hyaluronic acid fragments significantly improves the T

cell response and helps the dendritic cells to become more potent antigen presenting cells (page 17, lines 6-9 of the specification; page 20, lines 8-11, 19-22 of the specification).

In light of the above amendment and remarks, withdrawal of the rejection of claim 57 under 37 U.S.C. § 112 is respectfully requested. Applicants believe that claim 57, as amended, is fully supported by the disclosure, patentable over the prior art, and in condition for allowance.

**B. Rejections Maintained Under 35 U.S.C. § 102(b)**

In response to the Examiner's maintained rejection of claim 34 under 35 U.S.C. § 102(b) as being anticipated by Wenge *et al.*, without acquiescing in the rejection, and in accordance with the Examiner's suggestion on October 14, 2003, Applicants have amended claim 34 to recite hyaluronic acid fragments that are from 2,000-5,000 Da. Thus, the Examiner's rejection is hereby rendered moot by the Applicants' amendments.

In further support of the patentability of claim 34 over the prior art of Wenge *et al.* and Noble *et al.*, Applicants point out that the Declaration Under 37 C.F.R. § 1.132 of Dr. Jan Simon, a co-inventor of the instant invention, submitted with Applicants' response dated September 13, 2002, is objective evidence of the patentability of the claimed invention over the prior art. The Examiner is urged to consider the factual statements within the Declaration as objective evidence, which carry more weight than arguments alone. *See* M.P.E.P. § 716(c). The objective evidence submitted by Dr. Simon in paragraphs 4 and 5 of the Simon Declaration clearly states that the low molecular weight hyaluronic acid fragments of 2,000-5,000 Da are much smaller in size compared to the "at least about 750,000" Da hyaluronic acid fragments disclosed by Wenge *et al.* or the 200,000 Da hyaluronic acid fragments taught by Noble *et al.* Furthermore, Dr.

Simon states in paragraph 6 of the Declaration that the high molecular weight hyaluronic acid

fragments, such as those taught by Wenge *et al.* and Noble *et al.*, are completely ineffective to stimulate or mature dendritic cells, in contrast to the claimed invention. Thus, Applicants respectfully submit that neither Wenge *et al.* nor Noble *et al.* anticipate the claims of the claimed invention because these references fail to teach hyaluronic acid fragments that are from 2000-5,000 Da. Applicants believe that claim 34, as amended, is allowable over the prior art.

In response to the Examiner's rejection of claim 57 under 35 U.S.C. § 102(b) as being anticipated by Noble *et al.*, Applicants note that amended claim 57 depends from amended claim 34, which should be allowable. Thus, Applicants believe that claim 57, as amended and described above, is fully supported by the disclosure, patentable over the prior art, and in condition for allowance. No new matter has been added by these amendments. In light of the above remarks and arguments, withdrawal of the rejection of claims 34 and 57 under 37 U.S.C. § 102(b) is respectfully requested.

### **C. The Examiner's Objections**

In response to the Examiner's objections to claims 35-43 and 60 as being dependent upon a rejected base claim, Applicants respectfully remind the Examiner that claim 35 was canceled in the Applicants' Response and Amendment filed May 12, 2003. The Examiner's objection should therefore not apply to claim 35. Applicants believe that because claims 36-43 and 60 now depend upon allowable claim 34, as amended, claims 34, 36-43, and 60 are patentable over the prior art, and are in condition for allowance.

**V. Conclusion**

In light of the above amendments and comments, Applicants respectfully request that all rejections and objections be withdrawn and that a timely Notice of Allowance should be issued in this application. Should the Examiner have any questions, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

Date:

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By

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